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RESEARCH ARTICLE

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Effect of neuromuscular electrical stimulation and early physical activity on ICU-acquired weakness in mechanically ventilated patients: A randomized controlled trial

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Abstract

Background: Intensive care unit-acquired weakness (ICU-AW) is common in critically ill patients and increases the duration of mechanical ventilation (MV) and weaning time. Early mobilization, range of motion (ROM) exercises, and neuromuscular electrical stimulation (NMES) can prevent ICU-AW by maintaining muscle mass. However, studies highlighting the effects of combining NMES with early physical activity in ICU patients are limited.

Aim: To evaluate the effect of NMES and early physical activity on ICU-AW in mechanically ventilated patients.

Study Design: A single-blinded randomized controlled trial was conducted in Alexandria, Egypt. Patients were randomly assigned to one of four groups: NMES, ROM, combined therapy (ROM + NMES), or conventional care (control group). The Medical Research Council (MRC) scale was used to assess the ICU-AW for the study patients over a 7-day period. The duration of the patient's MV and ICU stays were recorded.

Results: Of the 180 patients who were assessed for eligibility, 124 were randomly assigned to one of four groups: 32 patients in ROM exercises, 30 in NMES, 31 in combined therapy (ROM + NMES), and 31 in the control group. On day 7, ROM + NMES and NMES groups showed higher MRC scores than ROM and control groups (50.37 ± 2.34, 49.77 ± 2.19, 44.97 ± 3.61, and 41.10 ± 3.84, respectively). ANOVA test results indicated significant differences ($p < .001$) across the four groups. ICU-AW occurred in 0% of the ROM + NMES group, 60% of the ROM group, 13% of the NMES group, and 100% of the control group ($p < .001$). The MV duration (in days) in the ROM + NMES group was shorter (12.80 ± 3.800) than in the ROM, NMES, or control groups (21.80 ± 4.460, 18.73 ± 4.748, and 20.70 ± 3.932, respectively). ICU-LOS was shorter in the ROM + NMES group (17.43 ± 3.17 days) compared with the ROM group (22.53 ± 4.51 days), the NMES group (21.10 ± 5.0 days), and the control group (21.50 ± 4.42 days) with significant differences ($p < .001$) between the four groups.

Clinical Trial registration number: ClinicalTrials.gov ID: NCT05465291.

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Conclusion: Daily sessions of NMES and early physical activity were well tolerated, preserved muscle strength, prevented ICU-AW, and decreased the duration of the MV and ICU stay.

Relevance to Clinical Practice: The findings of this study support the use of NMES and early physical exercises by critical care nurses as part of routine care for critically ill patients.

KEYWORDS
critically ill patients, intensive care unit-acquired weakness, mechanical ventilation, neuromuscular electrical stimulation, physical activity

1 | INTRODUCTION

Prolonged mechanical ventilation (MV) due to critical illness is commonly linked with intensive care unit-acquired weakness (ICU-AW), characterized by skeletal muscle wasting and weakness.[1–3] ICU-AW is linked to negative consequences such as delayed weaning from MV,[4] increased weaning failure with a higher risk of reintubation or tracheotomy, longer ICU and hospital stays,[5] and increased mortality rates.[6] The pathogenesis of ICU-AW is complex and diverse. Hyperglycaemia, immobilization, the use of neuromuscular blockers, and multiple organ failure are risk factors for ICU-AW.[7,8] ICU-AW occurs in 26%–65% of conscious patients on MV for 5–7 days.[9,10] Sepsis and systemic inflammatory response syndrome are associated with 70% of ICU-AW cases,[11] while 100% of patients with multiple organ failure are at risk of ICU-AW.[8] In addition, nursing costs are increased by 60% due to ICU-AW, placing a heavy financial and health care burden on hospitals and individual families.[12]

Since there are currently no fully efficient treatments for ICU-AW, prevention is a crucial component of care, especially in ICUs with limited resources.[10] ICU-AW prevention relies on nursing measures like positioning, active and passive range of motion (ROM) exercises, chair sitting, and walking. The preservation of muscle mass has been linked to nutritional assistance, early mobilization, respiratory physiotherapy, ROM exercises, massage, and neuromuscular electrical stimulation (NMES).[13,14] Therefore, methods and measures to decrease such problems in ICU patients become necessary. Critical care nurses (CCNs) can easily implement active or passive ROM exercises to help critically ill patients move during the treatment course.[15] ROM exercises affect muscles, joints, ligaments, fascia, arteries, and nerves. ROM exercises improve blood circulation, vascular dynamics, connective and joint tissue mobility, and synovial movement to nourish cartilage.[16]

Many research studies have been carried out to evaluate rehabilitation practices targeted at preventing ICU-AW in ICU patients. Dirks et al., Maffiuletti et al., and Nakanishi et al., found that NMES can prevent muscle atrophy in ICU patients.[17–19] NMES is a type of exercise and mobilization that can be used on immobilized patients without requiring active participation. NMES has been recommended as a substitute for early active mobilization for ICU patients who are unresponsive and uncooperative.[20,21] The goal of NMES is to restore functional movement by stimulating specific muscle groups via electrodes with a low-frequency current (typically 30–50 Hz).[22]

To date, there is no convincing evidence regarding the effect of NMES and physical activity on ICU-AW occurrence. Some studies have shown that NMES can minimize the risk of ICU-AW by strengthening muscles and reducing MV duration and ICU length of stay (ICU-LOS).[17,23] However, other studies have revealed that NMES has little impact on skeletal muscle mass in ICU patients.[24,25] Despite the fact that NMES has been considered an alternative approach for

What is known about the topic

- ICU-AW is a common neuromuscular complication of critical illness characterized by muscle weakness, a prolonged duration of weaning from MV, and a prolonged ICU and hospital stay.
- NEMS is a form of exercise that does not require the participation of the patient. Previous research indicates that NEMS has an acute systemic influence and helps critically ill patients preserve muscle mass.
- NMES has been proven to lower the risk of ICU-AW by strengthening muscles and lowering the MV and ICU length of stay. However, a number of studies have found that NMES does not significantly improve muscular strength in ICU patients.

What this paper adds

- According to the results of this study, daily sessions of NMES and physical activities for critically ill patients preserved muscular strength, decreased the duration of MV and ICU stays, and prevented the occurrence of ICU-AW to some extent.
- The current study indicated that NMES is a simple, well-tolerated intervention with no side effects.
- The study findings highlight the potential benefits of incorporating NMES and early physical activity into the nursing practice of mechanically ventilated patients.

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enhancing mobility in ICU patients,[26] it is questionable if its early application can prevent ICU-AW. A meta-analysis conducted by Liu et al.[22] indicated that three studies examined the effects of early NMES use in critically ill patients[18,27,28] but the evidence was ambiguous due to the studies' diversity and inconsistent findings. Furthermore, the most recent systematic review of randomized controlled trials by García-Pérez-de-Sevilla and Sánchez-Pinto Pinto[29] found that physical activity and NMES prevent excessive loss of muscle in patients admitted to the ICU and increase muscle strength in patients discharged with ICU-AW. However, it is important to note that this study does include limitations pertaining to inconsistencies that might potentially affect the validity of their risk of bias assessment. Despite studies demonstrating the effects of exercises in combination with NMES in COPD patients,[30,31] the effects of this connection in ICU patients remain unknown. More well-designed research studies are needed to validate the effect of NMES and physical activity in preventing ICU-AW.

2 | AIM OF THE STUDY

This study aims to evaluate the effect of NMES and early physical activity on ICU-AW in mechanically ventilated patients.

2.1 | Research hypothesis

Patients who receive NMES and early physical activity have a lower ICU-AW than patients in the control group who do not receive NMES or early physical activity.

3 | METHODS

3.1 | Research design and settings

A single-blinded randomized controlled trial was conducted on mechanically ventilated patients admitted to five general ICUs at a hospital in Alexandria, Egypt, which has a total of 58 ICU beds. The criteria for the Consolidated Standards of Reporting Trials (CONSORT) were met by this study.[32]

3.2 | Recruitment and eligibility

Over the course of 4 months, from October 18, 2022, to February 18, 2023, daily evaluations of new patients were conducted. The following inclusion criteria were set for study participation: aged ≥18 years, who was supposed to be on a mechanical ventilator ≥48 h, and spent in the ICU ≥4 days. Exclusion criteria: pre-existing neuromuscular disease, peripheral vascular diseases (arterial lower limb disease and deep venous thrombosis), hemiplegia/quadriplegia, lower limb amputation, spinal injuries, taking muscle relaxants, cognitive impairment, brain death, obesity (body mass index >35 kg/m^2), pregnancy, bone fractures, limb skin lesions, the presence of a cardiac pacemaker, or end-stage malignancy.

3.3 | Sample size

A minimum total sample size of 120 patients was sufficient to detect an effect size of 0.35 with a power ($1-\beta = 0.90$) of 90% at a significant probability level alpha of $p < .05$ partial eta squared of 0.11. Sample size estimations indicate 30 patients per treatment group (A1, A2, A3, and A4).The sample size was calculated according to G*Power software version 3.1.9.6.[33,34]

3.4 | Randomization, blinding, and allocation concealment

Patients were included in this trial within 24 h of being admitted to the ICU and were randomly allocated to one of four groups (A, B, C, or D) by utilizing a block randomization approach with an 8-block size. The patients' groups were labelled as follows: A for ROM exercises, B for NMES, C for ROM + NMES, and D for the control group. The randomization list was generated using free Internet software (https://www.sealedenvelope.com/simple-randomiser/v1/lists). Using opaque, sealed envelopes allowed for the concealment of the allocation. The envelopes were prepared by a research coordinator who was not involved in participant recruiting or evaluation. The envelopes contained a randomization card identifying the participant's treatment group assignment, which was given to the investigator only after the subject enrolled in the research. To reduce bias, the researcher recruited patients and assigned them to groups without seeing the randomization list. The researcher who recruited patients and assigned them to groups only had access to the group names (A, B, C, or D) and not the randomization list. The researcher who recruited and assigned patients did not participate in data collection or outcome evaluation. Due to the nature of the interventions being evaluated, blinding of patients and researchers involved in delivering the interventions was not possible in our study. The outcome assessor, who was responsible for assessing the study's outcomes, was blinded in order to reduce the possibility of bias. The outcome assessor was blinded to the intervention assignment, so she did not know which participants received the combined intervention and which received the control intervention. Finally, the researcher who analysed the data was unaware of the patients' group assignment.

3.5 | Research instruments

The researchers developed the ICU-AW assessment tool to track patients' reactions to NMES and physical activity throughout the course of the study and to record their muscle strengths and weaknesses. It had three parts: Part one included patients' bio-demographic

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and clinical information, such as their age, gender, diagnosis, comorbidities, APACHE II score, Richmond Agitation Sedation Scale (RASS), Body Mass Index (BMI), and ICU-LOS. Additionally, it contained laboratory biomarkers (i.e. HB, albumin, Na, K, Mg, phosphorus, calcium, and random blood sugar).

Part two covered patients' respiratory and hemodynamic parameters. This part monitored patients' haemodynamic and respiratory responses to NMES and physical activity throughout the study. Heart rate, systolic, diastolic, mean arterial, and peripheral oxygenation (SpO_2). Also, the following data were included: ventilation mode, tidal volume (Vt), fraction of inspired oxygen (FiO_2), positive end expiratory pressure (PEEP), minute ventilation, and pressure support. Patient data from admission to day 7 was recorded in a flow chart for this section.

Part three assessed ICU-AW using the Medical Research Council (MRC) scale.[4,35–37] The MRC scale assessed three muscle groups in each limb. For six lower and upper limb movements, the score ranges from 0 (no muscle contraction) to 5 (active movement against full resistance). Wrist and forearm flexion, shoulder abduction, ankle dorsiflexion, knee extension, and hip flexion were evaluated. Patients with ICU-AW had MRC scores of <48 out of 60, suggesting significant muscular weakness. When their MRC scores dropped to 36 out of 60, these patients had severe muscular weakness.[35]

3.6 | Data collection procedure

The study was initially registered at ClinicalTrials.gov with the primary outcomes measured on days three and five; however, based on clinical relevance, we decided to modify the duration of measurement to assess the occurrence of ICU-AW" on day seven compared with day 2. Furthermore, we observed that the average duration of MV in the study population was 7 days. We decided to measure the incidence of ICU-AW on day 7 rather than day 5 to capture the full effect of our intervention.

On the second day of admission, ICU patients were randomly allocated to one of four groups: ROM, NMES, NMES + ROM, or control. The ICU protocol for general clinical management (including nutrition and glycaemic control), ventilator support, and MV weaning was followed for all patients in the four groups from the second to the 7th day. The third author (who is a lecturer of physical medicine, rheumatology, and rehabilitation at the faculty of medicine at Alexandria University, Egypt) delivered and supervised the interventions (ROM and NMES) in order to maintain uniformity and adherence to the research protocol. The third author also trained research assistants (three nurses) on the study procedure to ensure that all participants received the same interventions.

The control group received conventional care according to the mobilization protocol of the ventilated patients in the study setting, which included changing postures every 2 h. For such a group of patients, the implementation of active or passive ROM exercises was minimal and only took place when a physician formally ordered them. Percussion and vibration were offered as a kind of respiratory therapy, but only during the morning shift. A physician may have prescribed chair sitting as an alternative to bed rest for a specific patient. However, adoption was hindered by obstacles including a shortage of staff, concerns about adverse events like falls, and higher nursing workloads. Physical therapist consultation and treatment were rarely offered when ordered by physicians.

The ROM group received passive/active ROM exercises, starting with passive limb ROM for nonresponsive patients and progressing to active for cooperative patients. Upper extremity ROM consisted of shoulder flexion, extension, abduction, elbow flexion and extension, and wrist flexion and extension. Exercises for the lower extremities' ROM included hip and knee flexion, hip extension, hip abduction, ankle dorsiflexion, and plantar flexion. Ten rhythmic repetitions of each movement were performed. The ROM exercises took 30–60 min and were performed between 3 and 7 p.m., when the ICU's workload was lower. Intolerance to ROM exercises was indicated by the presence of any of the following: oxygen saturation ≤88%, respiratory rate ≤5 or ≥30 cycles per minute, heart rate ≤40 or ≥130 beats per minute, arrhythmia, systolic blood pressure ≥200 mmHg, and mean arterial pressure ≤65 mmHg. In cases of intolerance, ROM exercises were postponed until the patient's condition stabilized.

Patients in the NMES group received the intervention from day 2 of ICU admission through day 7 utilizing a dual-channel NMES machine (Alph Wave Heatronic BM-1004, China). The NMES therapy was applied bilaterally to three muscle heads of the quadriceps muscle (rectus femoris, vastus medialis, and vastus lateralis) for 60 min daily. Hairy skin was properly shaved and cleansed before attaching the electrodes, and surface reusable gel (~5 × 10 cm [2 × 4 in] oval for quadriceps square) was placed at standardized electrode locations, adjusted to eliminate interference with heart monitors. To guarantee that the electrode positions remained constant throughout the intervention, all electrodes were fixed with elastic straps. Patients were positioned in a supine position with head elevation. To enable knee extension, a half-roll pillow was placed at the back of the knee. The legs were set neutrally, with 15° hip flexion and 30° knee flexion. Then, four electrodes were applied to each rectus femoris, vastus lateralis, and vastus medialis. For each muscle, we used the following NMES settings: pulsed-current, biphasic, asymmetrical, balanced rectangular waveform; ramp-up time of 2 s; ramp-down time of less than 1 s; frequency of 50 Hz; pulse duration of 400 μs; "on" period of 5 s; and "off" time of 10 s. The degree of muscular contraction was assessed by observing and palpating the contracted muscle. The daily 1-h session included 5-min warmups and 5-min recoveries.[38] In cases of confusion, muscular contraction has been verified by palpating the relevant muscles.

Patients in the NMES + ROM group received NMES pulse ROM exercises as described previously. NMES was applied at the same time that the limbs were being worked out.

3.7 | Outcome parameters

The primary outcomes included the occurrence of ICU-AW, which was assessed by the MRC scale. The fifth researcher, who did not participate in the intervention or randomization of the study sample, assessed muscle strength using the MRC scale from the first day of

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ICU admission and throughout the study period. For assessment and recording MRC, patients were checked daily for awakening and comprehension after sedation was discontinued according to the established clinical protocols of the study setting. The clinical staff regularly evaluated patients' clinical states, level of consciousness, and other physiological factors in order to gradually reduce and stop sedation. At least three responses to "open/close your eyes", "look at me", "put out your tongue", "nod your head", or "raise your eyebrows" were required to determine MRC.[39] The investigators were blind to the patient distribution. Data on secondary outcomes were recorded, such as duration of MV in days, level of agitation measured by RASS, level of consciousness, day of cooperation and ICU-LOS. Days of cooperation in our study refers to the number of days the patient actively engaged in the interventions. All patients' data were evaluated at the same time of day. To guarantee consistency in the period of data collection across all participants, data were gathered specifically between the hours of 3:00 and 7:00 p.m. This strategy was selected to reduce any variation in the data that could result from circadian rhythms or other time-of-day impacts. Potentially adverse events experienced by participants throughout the research were tracked and documented.

3.8 | Statistical analysis

The data were fed into the computer and analysed with the IBM SPSS software package, version 20.0 (Armonk, NY: IBM Corp.). The Kolmogorov–Smirnov test was used to confirm the data's normality and demonstrate that it was normally distributed. The mean and standard deviation were used to describe the quantitative data. The Chi-square test was used to compare categorical variables between groups. For normally distributed quantitative variables, the one-way ANOVA test was used to compare more than two groups. For normally distributed quantitative variables, the paired *t*-test was used to compare days 2 and 7. The significance of the obtained results was determined at a 5% level.

3.9 | Ethical approval and registration

The study received approval from Alexandria University's Faculty of Medicine Ethics Committee on 19 May 2022 (No. 0305579), and it was also registered with ClinicalTrials.gov (ID: NCT05465291). We received informed consent from conscious patients and each unconscious patient's legally authorized representative before enrolling them in the study. Patients or legally authorized representatives were informed about the study's objective, methods, possible risks and benefits, and their rights regarding participation. The confidentiality of the collected data was maintained, as was the patients' privacy. The patients also had the option to withdraw from the study whenever they wanted.

4 | RESULTS

A total of 180 patients were evaluated for eligibility. Based on the inclusion criteria, 53 patients were considered ineligible, while three declined

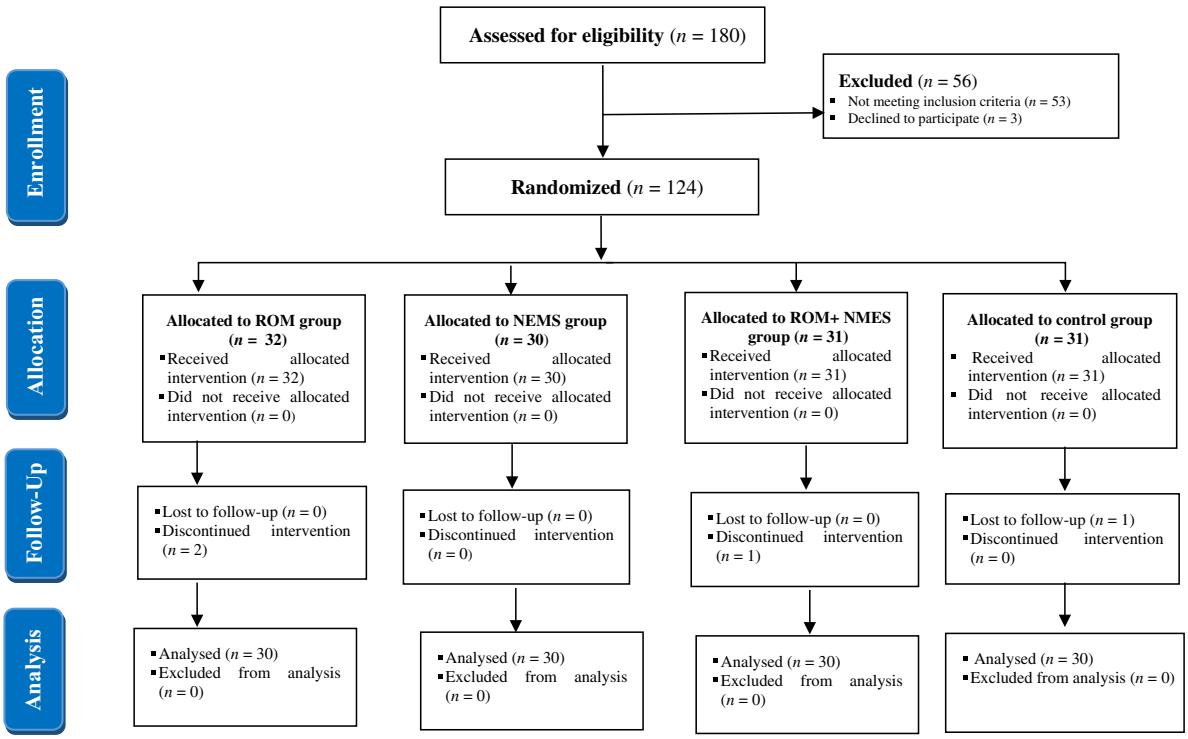
Enrollment
Allocation
Follow-Up
Analysis
Assessed for eligibility (n = 180)
Excluded (n = 56)
Not meeting inclusion criteria (n = 53)
Declined to participate (n = 3)
Randomized (n = 124)
Allocated to ROM group (n = 32)
Received allocated intervention (n = 32)
Did not receive allocated intervention (n = 0)
Allocated to NEMS group (n = 30)
Received allocated intervention (n = 30)
Did not receive allocated intervention (n = 0)
Allocated to ROM+ NMES group (n = 31)
Received allocated intervention (n = 31)
Did not receive allocated intervention (n = 0)
Allocated to control group (n = 31)
Received allocated intervention (n = 31)
Did not receive allocated intervention (n = 0)
Lost to follow-up (n = 0)
Discontinued intervention (n = 2)
Lost to follow-up (n = 0)
Discontinued intervention (n = 0)
Lost to follow-up (n = 0)
Discontinued intervention (n = 1)
Lost to follow-up (n = 1)
Discontinued intervention (n = 0)
Analysed (n = 30)
Excluded from analysis (n = 0)
Analysed (n = 30)
Excluded from analysis (n = 0)
Analysed (n = 30)
Excluded from analysis (n = 0)
Analysed (n = 30)
Excluded from analysis (n = 0)

FIGURE 1 CONSORT flow diagram of participants through the trial (figure can be viewed at wileyonlinelibrary.com). NEMS, neuromuscular electrical stimulation; ROM, range of motion.

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TABLE 1 Patients' baseline demographic and clinical characteristics in the ROM, NMES, ROM + NMES, and control groups.

Characteristic	Groups								Test of sig.	p
	ROM ($n = 30$)		NMES ($n = 30$)		ROM + NMES ($n = 30$)		Control ($n = 30$)			
Age (years) (mean ± SD)	45.57 ± 8.869		40.30 ± 9.252		38.80 ± 11.01		42.43 ± 13.153		$F = 2.203$	.091
Gender *n* (%)										
Male	16	(53.3)	15	(50.0)	16	(53.3)	14	(46.7)	$\chi^2 = 0.367$	.947
Female	14	(46.7)	15	(50.0)	14	(46.7)	16	(53.3)		
Admission diagnosis[a] *n* (%)										
Cardiovascular	8	(26.7)	9	(30.0)	10	(33.3)	11	(36.7)	$\chi^2 = 0.770$	.857
Respiratory	14	(46.7)	16	(53.3)	21	(70.0)	18	(60.0)	$\chi^2 = 3.649$	.302
Renal	3	(10.0)	7	(23.3)	9	(30.0)	7	(23.3)	$\chi^2 = 3.732$	.292
Gastrointestinal	3	(10.0)	2	(6.7)	1	(3.3)	1	(3.3)	$\chi^2 = 1.619$	$^{MC}p = 0.836$
Trauma	3	(10.0)	3	(10.0)	2	(6.7)	5	(16.7)	$\chi^2 = 1.583$	$^{MC}p = .737$
Neurological	10	(33.3)	5	(16.7)	5	(16.7)	3	(10.0)	$\chi^2 = 5.755$	.124
Comorbidities[a] *n* (%)										
Hypertension	19	(63.3)	20	(66.7)	13	(43.3)	17	(56.6)	$\chi^2 = 3.922$	.270
Diabetes	16	(53.3)	11	(36.7)	11	(36.7)	11	(36.7)	$\chi^2 = 2.587$	.460
Heart failure	2	(6.7)	4	(13.3)	4	(13.3)	8	(26.7)	$\chi^2 = 4.533$	$^{MC}p = 0.210$
Kidney diseases	0	(0.0)	0	(0.0)	0	(0.0)	1	(3.3)	$\chi^2 = 2.829$	$^{MC}p = 1.000$
COPD	7	(23.3)	9	(30.0)	7	(23.3)	13	(43.3)	$\chi^2 = 3.810$	0.283
Other	3	(10.0)	2	(6.7)	4	(13.3)	0	(0.0)	$\chi^2 = 4.425$	$^{MC}p = 0.248$
APACHE II score (mean ± SD)	29.83 ± 3.26		28.03 ± 4.42		29.90 ± 3.92		28.43 ± 3.96		$F = 1.795$	.152
BMI (kg/m^2) (mean ± SD)	30.17 ± 1.577		30.17 ± 2.601		30.27 ± 1.552		29.70 ± 3.543		$F = 0.317$	.813
RASS	−0.30 ± 0.88		−0.10 ± 0.92		−0.20 ± 0.89		−0.23 ± 0.82		$F = 0.271$	.846
Ventilator data										
Mode of MV *n* (%)										
PSV	11	(36.7)	18	(60.0)	15	(50.0)	17	(56.7)	$\chi^2 = 6.152$	$^{MC}p = 0.350$
SIMV	18	(60.0)	12	(40.0)	15	(50.0)	13	(43.3)		
Assist control	1	(3.3)	0	(0.0)	0	(0.0)	0	(0.0)		
Tidal volume (mean ± SD)	465.10 ± 35.69		454.80 ± 95.77		452.50 ± 94.75		426.60 ± 41.58		$F = 1.522$	.213
FIO2 (%) (mean ± SD)	71.70 ± 21.18		61.33 ± 14.32		61.33 ± 14.31		66.67 ± 20.06		$F = 2.356$	0.075
PEEP mmHg (mean ± SD)	5.80 ± 1.27		5.90 ± 0.845		5.80 ± 0.761		6.07 ± 0.868		$F = 0.519$	.670
Pressure support mmHg (mean ± SD)	12.70 ± 2.32		12.20 ± 0.961		12.13 ± 1.042		12.40 ± 0.968		$F = 0.932$	.428
Clinical biomarkers (mean ± SD)										
Haemoglobin	10.83 ± 1.915		11.24 ± 2.677		11.11 ± 2.778		11.84 ± 2.078		$F = 0.956$	.416
Haematocrit	41.09 ± 4.10		41.40 ± 4.24		41.70 ± 4.39		40.39 ± 3.41		$F = 0.576$	.632
Albumin	3.69 ± 0.62		3.62 ± 0.44		3.60 ± 0.49		3.77 ± 0.30		$F = 0.734$	.534
Sodium	145.07 ± 12.22		140.87 ± 5.53		140.20 ± 5.67		139.63 ± 2.92		$F = 1.492$	.220
Potassium	4.06 ± 0.66		3.88 ± 0.24		3.87 ± 0.22		3.84 ± 0.23		$F = 2.017$	.115
Calcium	10.23 ± 0.28		9.96 ± 1.24		9.73 ± 1.23		9.91 ± 1.21		$F = 1.085$	.358
Blood glucose	160.87 ± 79.05		172.13 ± 59.67		172.80 ± 59.0		159.20 ± 52.08		$F = 0.390$	.760

Abbreviations: APACHE II, Acute Physiology and Chronic Health Evaluation II; BMI, Body Mass Index; *F*, ANOVA test; FiO_2, fraction of inspired oxygen; MC, Monte Carlo; NEMS, neuromuscular electrical stimulation; PEEP, positive end expiratory pressure; PSV, pressure support ventilation; RASS, Richmond Agitation Sedation Scale; ROM, range of motion; χ^2, Chi square test.

[a]Multiple answers were allowed.

to participate. Thus, 124 patients were randomly assigned to one of four groups: 32 patients in ROM exercises, 30 in NMES, 31 in combined therapy (ROM + NMES), and 31 in the control group. After this, three patients in the ROM group and the combined therapy (ROM + NMES) group were excluded due to prolonged MV (28 days were considered as prolonged MV). The decision to exclude patients who received prolonged MV for

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TABLE 2 Comparison between the four groups related to vital signs and ventilator parameters throughout the study period.

Parameters	Time	Groups				Test of significance	
		ROM ($n = 30$)	NMES ($n = 30$)	ROM + NMES ($n = 30$)	Control ($n = 30$)	F	p
Vital signs parameters							
Heart rate (mean ± SD)	Day 2	107.10 ± 21.67	106.57 ± 19.61	103.93 ± 14.72	102.67 ± 22.37	0.342	.795
	Day 7	109.57 ± 18.62	108.0 ± 15.35	97.70 ± 10.21	104.37 ± 20.63	3.122	.029*
MAP (mean ± SD)	Day 2	94.97 ± 15.16	94.36 ± 17.82	93.86 ± 16.29	99.40 ± 12.71	0.795	.499
	Day 7	85.80 ± 8.86	84.53 ± 10.58	87.30 ± 10.68	106.03 ± 15.48	22.669	<.001*
CVP (mean ± SD)	Day 2	18.57 ± 3.16	17.53 ± 2.93	17.90 ± 2.67	17.23 ± 4.19	0.915	.436
	Day 7	16.03 ± 1.79	16.13 ± 0.82	14.30 ± 2.42	16.07 ± 0.58	9.418	<.001*
Respiratory rate (mean ± SD)	Day 2	26.17 ± 3.06	27.87 ± 4.67	27.60 ± 4.68	26.73 ± 5.98	0.830	.480
	Day 7	25.53 ± 2.57	20.60 ± 5.49	20.37 ± 5.80	30.83 ± 4.24	33.193	<.001*
Temperature (°C) (mean ± SD)	Day 2	37.31 ± 0.22	37.29 ± 0.31	37.43 ± 0.41	37.29 ± 0.22	1.457	.230
	Day 7	37.06 ± 0.08	37.25 ± 0.21	37.39 ± 0.23	37.06 ± 0.08	26.821	<.001*
SpO_2 (%) (mean ± SD)	Day 2	97.23 ± 1.41	97.50 ± 1.46	97.07 ± 1.44	97.37 ± 1.40	2.151	.098
	Day 7	96.83 ± 0.79	97.20 ± 0.71	97.93 ± 1.11	96.30 ± 1.15	15.279	<.001*
Ventilator parameters							
FiO_2% (Mean ± SD)	Day 2	66.63 ± 13.73	61.33 ± 12.79	61.67 ± 11.17	58.17 ± 12.35	$F = 2.333$	.078
	Day 7	54.17 ± 14.27	41.50 ± 7.09	42.67 ± 7.85	58.83 ± 13.81	$F = 17.335$	<.001*
Minute volume L/min (Mean ± SD)	Day 2	13.26 ± 1.35	13.83 ± 2.54	13.90 ± 1.92	12.96 ± 0.82	$F = 1.932$	.128
	Day 7	13.03 ± 1.09	13.05 ± 1.58	12.29 ± 0.86	12.49 ± 0.93	$F = 3.363$	.021*
PEEP	Day 2	5.87 ± 0.73	5.90 ± 0.84	5.80 ± 0.76	6.07 ± 0.87	$F = 0.599$	.617
	Day 7	7.10 ± 0.76	6.13 ± 0.43	6.13 ± 0.43	6.23 ± 0.57	$F = 20.692$	<.001*
Pressure support	Day 2	15.93 ± 3.10	14.80 ± 3.10	14.97 ± 1.50	14.83 ± 1.97	$F = 1.590$	.196
	Day 7	14.30 ± 1.21	13.01 ± 1.01	13.01 ± 1.01	13.47 ± 1.54	$F = 7.585$	<.001*

Abbreviations: CVP, central venous pressure; F, ANOVA test; FiO_2, fraction of inspired oxygen; MAP, mean arterial pressure; NEMS, neuromuscular electrical stimulation; P, comparison between the four groups (ROM, NMES, ROM + NMES, and control); PEEP, positive end expiratory pressure; ROM, range of motion; SpO_2, peripheral oxygen saturation.
*Statistically significant at $p \leq .05$.

28 days from our study was made due to the possibility of complications associated with critical illness and prolonged immobilization. These variables may confound the effects of the intervention that our study is evaluating. By excluding patients with prolonged MV, we intended to reduce the influence of these confounding variables on the outcomes of interest. Furthermore, one patient in the control group died before discharge (Figure 1). As illustrated in Table 1, there were no significant demographic or baseline differences between the control and the three intervention groups (ROM, NMES, and ROM + NMES). Upon admission, there were no significant differences in age ($F = 2.203$; $p = .091$), gender ($\chi^2 = 0.367$; $p = .947$), APACHE II score ($F = 1.795$; $p = .152$), BMI ($F = 0.317$; $p = .813$), RASS ($F = 0.271$; $p = .846$), mode of MV ($\chi^2 = 6.152$; $p = .350$), potassium ($F = 2.017$; $p = .115$), blood glucose ($F = 0.390$; $p = .760$), haematocrit ($F = 0.576$; $p = .632$), or haemoglobin ($F = 0.956$; $p = .416$). Also, there were no significant differences between the four groups in terms of diagnoses and comorbidities upon admission to the ICUs.

As shown in Table 2, no statistically significant differences in vital sign parameters (HR, MAP, CVP, RR, Temp., and SpO_2) were observed on day 2 between the four groups ($F = 0.342$; $p = .795$, $F = 0.795$; $p = .499$, $F = 0.915$; $p = .436$, $F = 0.830$; $p = .480$, $F = 1.457$; $p = .230$, $F = 2.151$; $p = .098$, respectively). However, on day 7, a statistically significant difference in HR ($F = 3.122$; $p = .029$), MAP ($F = 22.669$; $p < .001$), CVP ($F = 9.418$; $p < .001$), RR ($F = 33.193$; $p < .001$), temperature ($F = 26.821$; $p < .001$), and SpO_2 ($F = 15.279$; $p < .001$) was found between the four groups.

Furthermore, Table 2 shows that there was a statistically significant difference between the four groups on the seventh day of MV in terms of FiO_2, minute volume, PEEP, and PS ($F = 17.335$; $p < .001$, $F = 3.363$; $p = .021$, $F = 20.692$; $p < .001$, $F = 7.585$; $p < .001$ respectively).

4.1 | Primary outcome measures

Table 3 shows that the four groups' mean MRC scores did not differ at day 2 ($F = 1.792$; $p = .152$), but they did at day 3 and throughout day 7 ($F = 25.187$; $p < .001$, $F = 60.130$; $p < .001$,

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TABLE 3 Comparison between the four studied groups regarding total MRC over the study period.

	Groups				Test of significance	
Total MRC/Time	ROM ($n = 30$)	NMES ($n = 30$)	ROM + NMES ($n = 30$)	Control ($n = 30$)	*F*	*p*
MRC (mean ± SD) Day 2	50.13 ± 1.17	50.97 ± 1.83	50.73 ± 2.07	50.03 ± 2.20	1.792	.152
MRC (mean ± SD) Day 3	47.47 ± 1.55	51.30 ± 2.55	50.77 ± 2.24	47.03 ± 3.03	25.187	<.001*
MRC (mean ± SD) Day 4	46.40 ± 2.86	50.70 ± 2.31	50.73 ± 2.26	44.87 ± 3.52	34.866	<.001*
MRC (mean ± SD) Day 5	45.80 ± 3.59	50.23 ± 2.21	50.53 ± 2.19	43.0 ± 4.19	39.641	<.001*
MRC (mean ± SD) Day 6	45.43 ± 3.73	49.90 ± 2.09	50.47 ± 2.27	41.83 ± 3.68	53.625	<.001*
MRC (mean ± SD) Day 7	44.97 ± 3.61	49.77 ± 2.19	50.37 ± 2.34	41.10 ± 3.84	60.130	<.001*

Abbreviations: *F*, ANOVA test; MRC, Medical Research Council; NEMS, neuromuscular electrical stimulation; P, comparison between the four groups (ROM, NMES, ROM + NMES, and control); ROM, range of motion.
*Statistically significant at $p \leq .05$.

FIGURE 2 Mean change of MRC over the study period in the four studied groups.

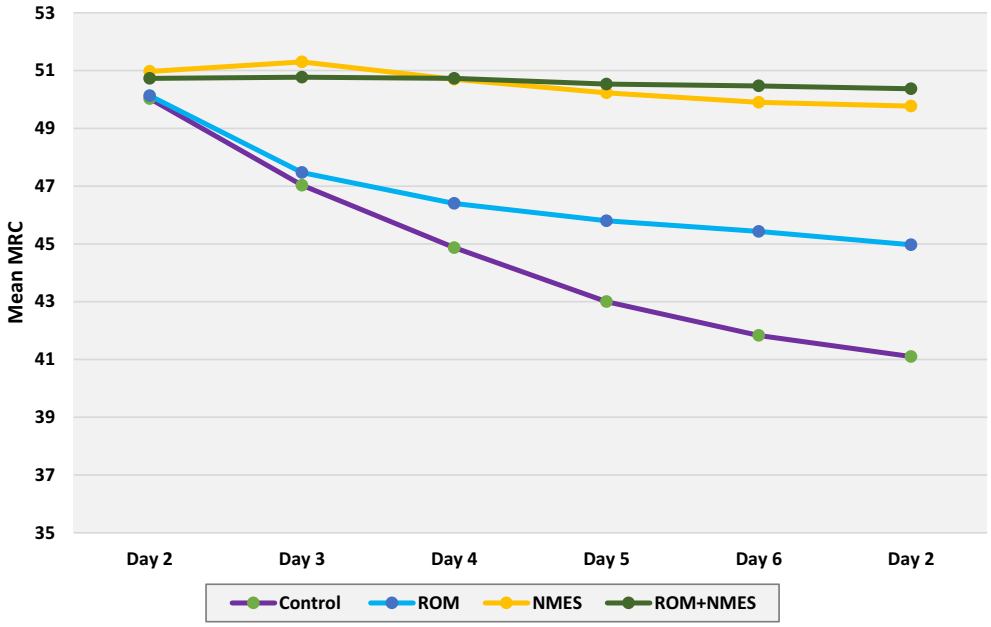

TABLE 4 Comparison between the four studied groups regarding primary outcomes throughout the study period.

		Groups				Test of significance	
Outcomes variables	Time	ROM ($n = 30$)	NMES ($n = 30$)	ROM + NMES ($n = 30$)	Control ($n = 30$)	Test	P1
MRC (mean ± SD)	Day 2	50.13 ± 1.17	50.97 ± 1.83	50.73 ± 2.07	50.03 ± 2.20	$F = 1.792$	.152
	Day 7	44.97 ± 3.61	49.77 ± 2.19	50.37 ± 2.34	41.10 ± 3.84	$F = 60.130$	<.001*
t (P2)		7.580 (<0.001*)	3.168 (0.004*)	1.690 (0.102)	12.829 (<0.001*)		
Percent change		−10.29%	−2.35%	−0.71%	−17.85%		
ICUAMW (MRC <48) *n* (%)	Day 7	18 (60.0)	4 (13.3)	0 (0.0)	30 (100.0)	$\chi^2 = 76.561$	<.001*

Abbreviations: *F*, ANOVA test; ICUAMW, ICU acquired muscle weakness; MRC, Medical Research Council; NEMS, neuromuscular electrical stimulation; P1, comparison between the four groups; P2, comparison between 2nd and 7th day in the same group; ROM, range of motion; χ^2, Chi square test; *t*, Paired *t*-test.
*Statistically significant at $p \leq .05$.

respectively). Both the control and ROM groups had MRC scores below 48 from day 3 to day 7. Throughout the study, the NMES and ROM + NMES groups' mean MRC scores were above 48. On the 7th day, the ROM + NMES and NMES groups had higher MRC scores than the ROM and control groups (50.37 ± 2.34, 49.77 ± 2.19 vs. 44.97 ± 3.61, and 41.10 ± 3.84, respectively). The results of the

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TABLE 5 Comparison between the four studied groups regarding secondary outcomes throughout the study period.

Outcomes variables	Time	Groups				Test of significance	
		ROM ($n = 30$)	NMES ($n = 30$)	ROM + NMES ($n = 30$)	Control ($n = 30$)	Test	p
RASS	Day 2	−0.30 ± 0.88	−0.10 ± 0.92	−0.20 ± 0.89	−0.17 ± 0.87	0.263	.852
	Day 7	0.23 ± 1.10	0.07 ± 0.83	0.80 ± 0.89	0.07 ± 1.44	3.054	.031*
GCS	Day 2	11.63 ± 1.13	11.37 ± 1.40	11.13 ± 1.31	11.30 ± 1.42	$F = 0.746$	.527
	Day 7	12.50 ± 1.76	11.50 ± 1.57	12.50 ± 1.76	11.50 ± 1.57	$F = 3.602$	.016*
MV duration days (Mean ± SD)		21.80 ± 4.460	18.73 ± 4.748	12.80 ± 3.800	20.70 ± 3.932	$F = 26.694$	<.001*
Day of cooperation (Mean ± SD)		3.13 ± 1.17	3.97 ± 1.52	3.67 ± 1.47	3.97 ± 1.40	$F = 2.377$	.073
ICU-LOS days (Mean ± SD)		22.53 ± 4.51	21.10 ± 5.0	17.43 ± 3.17	21.50 ± 4.42	$F = 7.918$	<.001*

Abbreviations: F, ANOVA test; GCS, Glasgow coma scale; ICU-LOS, Intensive Care Unit length of stay; MV, mechanical ventilation; NEMS, neuromuscular electrical stimulation; P, comparison between the four groups (ROM, NMES, ROM + NMES, and control); RASS, Richmond Agitation Sedation Scale; ROM, range of motion.
*Statistically significant at $p \leq .05$.

ANOVA test showed statistically significant differences ($F = 60.130$; $p < .001$) among the four groups.

Figure 2 shows that NMES and ROM + NMES patients had higher mean MRC scores throughout the study than ROM and control patients, even though the four groups were similar at baseline. Nevertheless, there were no clear differences between NMES alone and ROM + NMES in terms of MRC scores, as seen in Table 3 and Figure 2. Table 4 compares the four groups' MRC mean scores from the 2nd to the 7th days of MV. The control group had the lowest MRC value, falling 17.85% from day 2 to day 7, while the ROM + NMES group fell 0.7%. ICU-AW occurred in 0% of the ROM + NMES group, 60% of the ROM group, 13% of the NMES group, and 100% of the control group ($\chi^2 = 76.561$; $p < .001$). The results showed that NMES and early physical activity were well tolerated with no side effects; only two patients felt a prickling sensation during NEMS, but this was not clinically significant.

4.2 | Secondary outcomes measures

Table 5 illustrates that the RASS mean scores on day 2 did not differ significantly among the four groups ($F = 0.263$; $p = .852$), but on day 7, the ROM + NMES group exhibited a notably higher score (0.80 ± 0.89), and statistical analysis revealed significant differences between the four groups ($F = 3.054$; $p = .031$). On day 7, GCS improved in the ROM and ROM + NMES groups compared with the NMES and control groups, and the differences between the four groups were significant ($F = 3.602$; $p = .016$). No significant differences were observed in the days of cooperation between the four groups ($F = 2.377$; $p = .073$). It was found that the MV duration in the ROM + NMES group was shorter (12.80 + 3.800) than in the ROM, NMES, or control groups (21.80 ± 4.460, 18.73 ± 4.748, and 20.70 ± 3.932, respectively). Statistical analysis also indicated significant differences ($F = 26.694$; $p < .001$) across the four groups. Overall, ICU-LOS was shorter in the ROM + NMES group (17.43 ± 3.17 days) compared with the ROM group (22.53 ± 4.51 days), the NMES group (21.10 ± 5.0 days), and the control group (21.50 ± 4.42 days). The differences between the four groups were statistically significant ($F = 7.918$; $p < .001$).

5 | DISCUSSION

Our study found that daily consecutive NMES and/or ROM sessions preserved muscle strength as measured by MRC and reduced the incidence of ICU-AW compared with conventional care. Despite the lack of clear differences in ICU-AW incidence between the NMES and ROM+NMES groups, it is important to recognize that both interventions showed promise in preserving muscle strength and reducing the overall occurrence of ICU-AW compared with conventional care. The combined approach of NMES and ROM exercises may have synergistic effects, even if the specific effect on ICU-AW was not statistically distinguishable between the two groups. Vanderthommen and Duchateau[40] claim that the effects of NMES and voluntary muscular contractions during ROM exercises, as well as the differences in motor drive involvement between the two therapies, make these two modes more effective. They recommended passive exercise and NMES for bedridden, non-cooperative patients. It is evident that the early initiation of physical activity increases the opportunity to improve motor recruitment, nerve function recovery, and muscle strength. NMES may be used to generate a muscle contraction when the patient is unable to do so voluntarily, allowing for effective exercise and muscular endurance. As long as the patient remains unresponsive, passive ROM may be utilized in conjunction with the NMES. When the patient is ready, active ROM and voluntary contractions may be added to the NMES.[41]

The MRC evaluated all patients in our study on the second day after MV, which was consistent across the four groups. Beginning on day 3, MRC values in the ROM and control groups were less than 48, the cutoff value for diagnosing ICU-AW. The steady decline in MRC values among these groups of patients indicates that muscle wasting started out quickly and got worse over time. This might be a result of hypermetabolism, which is characterized by increased energy

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expenditure and excessive protein loss, primarily due to the breakdown of skeletal muscle.[42,43] The favourable findings seen in our study may be attributed to the implementation of early physical activity either by use ROM or/and NMES. The NMES also serves as an anabolic stimulus to the muscle and reverses the catabolic consequences of critical illness and immobilization.[44]

Our study's findings align with those of a previous study by Maffiuletti et al.[18] which found that ICU patients who received NMES in addition to standard care had better muscle strength compared with those who received sham stimulation or standard care alone. Also, the current study confirms the findings of Leite et al.[45] Patsaki et al.[46] Rodriguez et al.[47] and Chen et al.[48] which showed that the NMES intervention improved ICU patients' muscle strength more than the control group. In addition, our results match with a study done in Egypt by Abu-Khaber[49] who reported that MRC values were lower than 48 in both NMES and control groups beginning on day 3 after MV. The Routsi[38] study conducted in Greece showed that MRC was better in the NMES group than in the control group, but it was different from our results in that MRC was higher in both groups. The two studies' patients had different baseline characteristics, which explains the difference. Our patients were much sicker than Routsi's, as evidenced by our high Apache II score, which explains the relationship between ICU-AW development and illness severity. The vastus intermedius and rectus femoris of the quadriceps muscle's cross-sectional diameter were evaluated in another study in Greece by Gerovasili[50] to determine the muscle mass. These results match ours, even though our study used MRC as a clinical score and Gerovasili's used ultrasound as a radiological assessment.

However, some studies have shown that NMES does not significantly increase the muscular strength of ICU patients.[24,25] In this context, a systematic review and meta-analysis of randomized controlled trials conducted by Zayed et al.[51] concluded that NMES combined with conventional care did not lead to significant changes in muscular strength. Nakanishi et al.[19] also found that a 5-day NMES-mobilization protocol did not improve muscle strength or prevent ICU-AW in ICU patients.

We found that patients who received NMES together with ROM exercises had shorter MV durations and total ICU-LOS than those who received NMES alone, ROM exercises alone, or conventional care. One of the reasons for these outcomes may be the reduction of the inflammatory response induced by the using of NMES together with ROM exercises. It is well known that the severe inflammation that critically ill patients develop contributes to their deteriorating clinical condition. In addition to inflammation-induced hypermetabolism, increased protein catabolism and overburden of kidney and cardiac function also occur. This interpretation was confirmed by a study conducted by Akar et al.[52] in Turkey, who found that patients who received NMES in conjunction with active exercise had a lower inflammatory response during the period of MV compared with those who got NMES alone. They reported that Interleukin 6 levels decreased in the group receiving NMES combined with exercise, whereas interleukin 8 levels decreased in groups receiving NMES alone or in conjunction with exercise. These findings indicate that NMES does not increase the risk of an inflammatory response in ICU patients. In addition, our results further suggesting a link between limb and respiratory muscle weakness. Acute systemic effects after a single NMES session have been reported. NMES may reduce MV duration by releasing myokines into the systemic circulation, which may affect other muscles like the diaphragm.[44] Routsi et al.[38] found that patients in the NMES group weaned faster than those in the control group, supporting the link between limb and respiratory muscle weakening.

In addition, it has been demonstrated that the NMES and ROM exercises improves muscle strength and function and reduces muscle atrophy and weakness in immobile, critically ill patients. Improving physical performance may allow patients to tolerate weaning from MV earlier, reducing the requirement for MV and ICU care. Schweickert et al.[53] investigated early physical therapy in mechanically ventilated patients. Over 100 ventilated patients were randomized to control or early physical intervention. Physical activity decreased delirium and extended ventilator-free days over 28 days. Our findings are comparable with those of Dos Santos et al.[54] who reported that NMES and ROM exercises decreased MV time by 9 days compared with usual care. In addition, these findings are in agreement with previous research conducted by Leite et al.[45] and Chen et al.[48] which also illustrated the effectiveness of NMES interventions in reducing the ICU-LOS. Routsi et al.[38] on the other hand, were unable to demonstrate that the NMES group had a shorter MV duration. Although Routsi et al. observed that the NMES group had a shorter ICU-LOS than the control group, the difference was not statistically significant. Moreover, Zayed et al.[51] reported that the combination of NMES with usual care did not significantly reduce the ICU-LOS for critically ill patients.

We noted an improvement in RASS scores in the group of NMES with ROM compared with the control group. This could be due to the direct effects of NMES and ROM exercises on physical function as well as the calming effects of NMES on the central nervous system. Additionally, this outcome may be explained by the rising Glasgow coma score level in the combined ROM exercises and NMES.

In the current study, the combination of NMES and early physical activity led to better clinical outcomes and was well tolerated with no side effects. This was evident by the stabilization of safety parameters like HR, RR, MAP, CVP, SpO_2, FiO_2, and PEEP levels. Only two patients felt a prickling sensation during NEMS, but this was not clinically significant. The results are consistent with previous research[38,49] However, Segers et al.[23] examined the safety of NMES in critically ill patients. The only noticeable change was skin hyperaemia in 50% of patients following electrode removal, which gradually subsided. Additionally, there were no complaints of discomfort that prevented the intervention.

It is imperative to acknowledge that the outcomes seen in our study were anticipated to some extent based on the current body of literature. Prior to our research, various national[49] and international studies[38,45–48,53] examined how physical activity and NMES affect ICU-AW. These studies reported a positive effect on reducing the incidence of ICU-AW. However, most of these studies apply each intervention separately. Our research examined whether combining these two strategies would generate better results than a single intervention. This combination in our study resulted in better clinical

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outcomes, as evidenced by the shorter duration of MV and ICU-LOS. To the best of our knowledge, such effects have never been reported in high-quality ICU studies. While there is a lack of high-quality studies conducted in ICUs that specifically demonstrate the same magnitude of outcomes as those obtained in our study, existing literature suggests that both physical exercise and electrical stimulation have a beneficial impact on preventing ICU-AW.

Nevertheless, it is important to acknowledge that our findings show that, in terms of preventing ICU-AW, the addition of ROM exercises to NMES did not provide a clear difference compared with NMES alone. While the combination of NMES and ROM exercises may have potential advantages in terms of holistic rehabilitation, our study did not show clear evidence of superiority when it came to reducing ICU-AW. This may be due to the relatively small sample size. This limitation may have influenced the ability to detect small but clinically significant differences between the NMES and ROM+NMES groups. Future studies with larger sample sizes and more comprehensive outcome measures are warranted to provide a more conclusive understanding of the comparative effectiveness of these interventions.

Importantly, the processes by which physical activity and NMES prevent ICU-AW have been thoroughly investigated. Physical activity strategies, such as passive ROM exercises, have been shown to improve muscle strength, endurance, and function, which can prevent muscle atrophy and wasting caused by immobility in the ICU.[53,54] For instance, a study by Hosseini et al.[55] revealed that passive ROM exercises significantly improved motor function in stroke patients' upper and lower extremities. NMES, however, may stimulate muscles and prevent atrophy during immobility. Nakanishi et al.[19] shown that NMES reversed muscular atrophy in both the upper and lower limbs of critically ill patients. Similarly, Nakamura et al.[56] in Japan suggested that NMES has the possibility of preventing muscle volume loss in critically ill patients. In addition, Routsi et al.[38] found that daily NMES sessions can prevent polyneuromyopathy and shorten weaning in ICU patients. We believed that combining these two therapies would maximize benefits and enhance critically ill patients' outcomes.

5.1 | Limitations of the study

The study's limitations must be considered when interpreting its results. First, the study only had a short-term follow-up period of 7 days, and it is unclear whether there were any long-term clinically significant differences between the intervention and control groups. Future studies with long-term follow-up are needed. Second, while manual muscle testing is a reliable method for comprehensive assessment, the subjective nature of the MRC score may introduce an uncontrollable factor. Thus, further studies are needed to assess the muscle strength of critically ill patients using objective measurement tools such as the handgrip dynamometer. Thirdly, our study only evaluated the effects of NMES on muscle strength and did not assess its effects on muscle function or the patient's ability to perform activities of daily living. Finally, we initially registered the study at ClinicalTrials.gov with main outcomes assessed on days 3 and 5, but based on clinical relevance; we changed the length to evaluate ICU-AW on day 7 compared with day 2. We decided to measure the incidence of ICU-AW on day 7 rather than day 5 to capture the full effect of our intervention.

6 | CONCLUSION AND PRACTICE IMPLICATIONS

Findings of our study indicated that both NMES alone and the combination of NMES with ROM exercises have a positive effect on reducing ICU-AW and shortening the duration of MV and ICU-LOS to some extent. This finding emphasizes the potential benefits of incorporating these interventions into the nursing practice of critically ill patients. However, it is important to note that there were no clear differences in ICU-AW between the NMES and ROM+NMES groups based on the main outcome measure. Further research can build upon these findings to explore the comparative effectiveness of NMES alone versus NMES combined with ROM exercises in reducing ICU-AW.

AUTHOR CONTRIBUTIONS

Sahar Younes Othman: conceptualization, methodology, project administration, analysis and interpretation of data, writing the original and final manuscript drafts, writing-review and editing, visualization, and supervision. **Maysa Abdalla Elbiaa**: assisted with data collection, results preparation, analysis and interpretation of data. **Eman R. Mansour**: conceptualization, methodology, supervision, validation, and analysis & interpretation of data. **Ahmed M. El-Menshawy**: Investigation, validation, and writing-review & editing. **Shimmaa Mohamed Elsayed**: Assisted with data collection, results preparation, analysis and interpretation of data, and writing the original draft. All authors have reviewed and approved the final manuscript before submission.

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DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available on request from the corresponding author. The data are not publicly available due to privacy or ethical restrictions.

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